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WHAT'S NEW IN INTENSIVE CARE

How to set the ventilator during surgery? Key principles to guide intraoperative mechanical ventilation

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More than 230 million patients undergo general anesthesia with mechanical ventilation (MV) every year worldwide [1]. Millions develop postoperative pulmonary complications (PPC), substantially driving perioperative mortality. Optimum invasive ventilation for patients undergoing major surgery has been identified a top research priority in perioperative medicine [2]. Compared to the intensive care unit (ICU), patients in the operating room (OR) experience shorter periods of exposure and often present with healthier lungs and more favorable respiratory system mechanics. Ventilation practices, therefore, still differ between the OR and critical care setting [3]. This article highlights key principles and the relevance of intraoperative ventilator settings in the light of insights on intraoperative MV.

In the absence of positive end-expiratory pressure (PEEP), high tidal volumes (Vt, ≥ 10 ml/kg) improve patient oxygenation. This observation from 1963 by H.H. Bendixen formed the basis for decades of MV using high Vt in the OR and ICU. In 2013, the IMPROVE trial demonstrated that intraoperative ventilator settings impact postoperative complications: lowering the Vt together with application of PEEP reduced PPC and extrapulmonary complications by 60% after elective major abdominal surgery [4]. These findings were followed by a debate about relevant ventilator settings—most notably Vt and PEEP. The subsequent PROVILHO and PROBESE trials investigated high (12 cmH_2O) versus low (2–4 cmH_2O) intraoperative PEEP but found no differences in proportion of patients with postoperative complications between both groups [5, 6]. Then a large trial from Australia reported no difference in PPC between patients receiving low (6 mL/kg PBW) versus high (10 mL/kg PBW) Vt with the same levels of PEEP (5 cmH_2O) [7]. At the same time, studies among critically ill patients without acute respiratory distress syndrome (ARDS) did not find a benefit of low to very low tidal compared to moderate tidal volumes [8]. These findings posed the question how a strategy of low Vt with application of PEEP can be effective when neither intervention on its own impacted patient outcomes?

Observations from the ICU clarify these seemingly contradictory observations. In 2015, Amato et al. introduced the concept of driving pressure (DP = plateau pressure-PEEP) as a key predictor of ventilator-induced lung injury and mortality. DP, as an index sizing Vt to the "functional" size of the lung, reflects the interplay between PEEP, Vt, and respiratory system compliance (Crs). Ventilation of patients with identical Vt yields different DP when they have different Crs. This has important implications for intraoperative MV—the effects of setting intraoperative low Vt are completely mediated through a net reduction in intraoperative DP [9]. Importantly, this means for clinicians that using low Vt will only be effective if they lead to lower DP. Indeed, the effectiveness of low Vt has been shown to be compliance-dependent, with benefits mainly in patients with lower Crs (i.e., high elastance) [10]. The concept further explains why an intraoperative strategy combining lower Vt and PEEP can be so effective, as indicated by the IMPROVE trial: PEEP prevents cyclic (de-)recruitment and limiting Vt avoids overdistension, thereby optimizing intra-tidal compliance (Fig. 1, panel A), characterized by a shift of the

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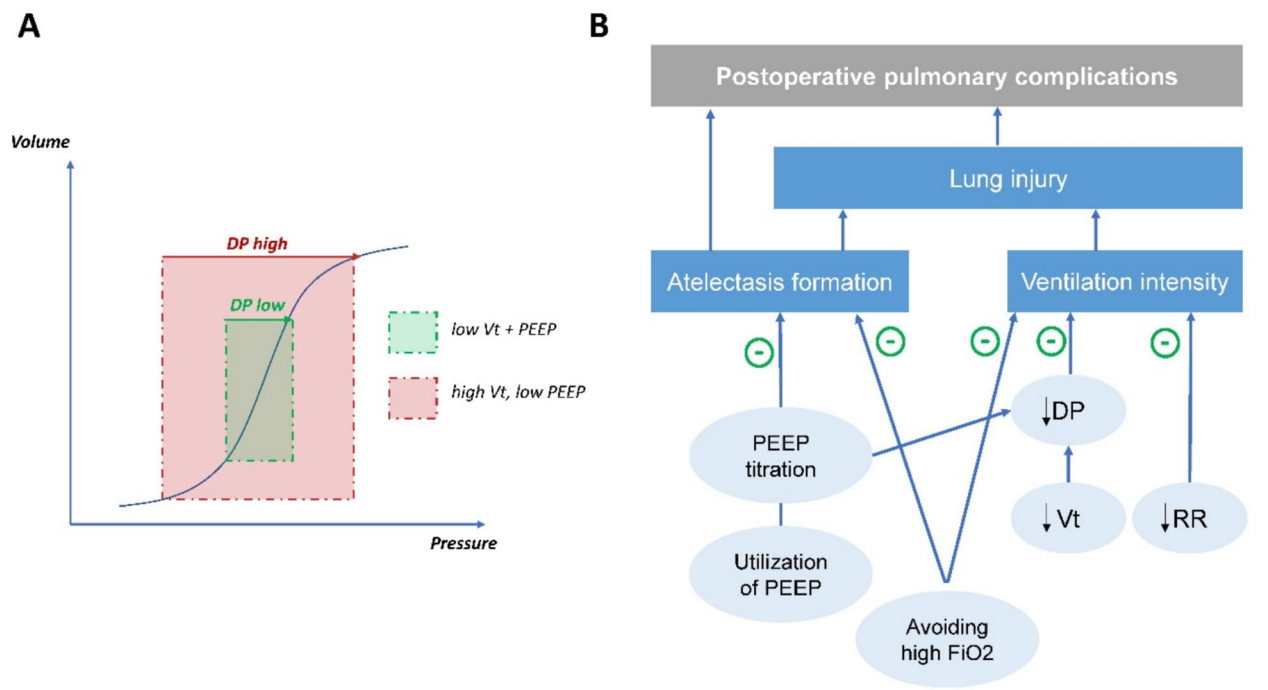

Fig. 1 Strategies to promote lung protective mechanical ventilation in the operating room include adaptation of tidal volume (Vt) and positive end-expiratory pressure (PEEP) to optimize the compliance of the respiratory system during each breath (intra-tidal compliance). Ideally, this results in a shift of the inspiratory phase to the steep (high-compliance) part of the pressure/volume curve (panel **A**). Panel **B** displays the underlying rationale of modulation of key drivers of ventilation intensity including driving pressure (DP), respiratory rate (RR), and inspiratory oxygen concentration (FiO_2) to avoid postoperative pulmonary complications

inspiratory phase to the steep part of the pressure/volume curve. Indeed, the difference in DP in the IMPROVE trial was much larger than in studies manipulating single parameters [4, 7].

Still, a PEEP of 5 cmH_2O, which has become standard during general anesthesia, is commonly inadequate intraoperatively, with 77% of patients showing signs of intra-tidal recruitment [11]. Individualized PEEP consistently improves oxygenation during intraoperative MV, especially during one-lung ventilation and can contribute to reduce PPC [12, 13]. In standard two-lung ventilation, the benefits of intraoperative PEEP individualization remain controversial. The original iPROVE trial, testing the effectiveness of intraoperative PEEP titration and postoperative continuous positive airway pressure, found no difference in proportion of patients with overall postoperative complications [14]. The recently published IMPROVE-2 trial showed that a strategy of individually adjusted highest PEEP targeting a DP below 13 cmH_2O did not reduce the incidence of PPC or death compared with a fixed PEEP of 5 cmH_2O [15]. Very recently, the DESIGNATION trial found no difference in PPC between a DP-guided, high-PEEP and a low-PEEP (5 cmH_2O) strategy among patients undergoing open abdominal surgery; however, DP separation between the groups was minimal (8 versus 10 cmH_2O) and most patients maintained a DP considered to be "safe" [16]. These findings carry important implications. First, a single DP target may be too simplistic, not reflecting true functional lung size for all patients. Second, responsiveness to optimum PEEP may be heterogeneous, as there is strong evidence to support PEEP individualization for one-lung ventilation [12]. It is important to avoid conflating "no benefit overall" with "no benefit for anyone".

For a long time, the rate of repetition (i.e., respiratory rate, RR) has been overlooked as an important contributor to PPC. In non-cardiothoracic surgery, a higher intraoperative RR, higher minute-ventilation, and downstream effects including hypocapnia have been linked to higher risks of PPC [17]. RR-induced hypocapnia may further exacerbate lung injury through ergotrauma [18]. A nascent concept integrating the inspiratory strain from Vt, stress from DP and repetition from RR is mechanical power, which aims to depict the overall intensity of MV and has been associated with higher risk of postoperative respiratory failure and critically ill patients even in the absence of ARDS [19]. Compensatory increases in RR can still increase ventilation intensity even when

Vt is reduced, especially among surgical patients with preserved lung compliance where lowering Vt has limited impact on DP. Indeed, when transitioning from the OR to the ICU, a common strategy of reducing Vt and increasing RR is associated with a higher risk of mortality through increased mechanical power [3]. Although mechanical power may help clinicians balance Vt, DP, and RR, there is uncertainty of how to operationalize the concept, particularly the inclusion of PEEP [20] and normalization to functional lung size [21]. Importantly, prospective evaluation in perioperative care is still lacking. Until further evidence emerges, targeting low DP (and, by analogy, high Crs) remains a key strategy to prevent avoiding intraoperative lung injury. Mechanical power might help guide clinicians choose between a low-Vt versus low-RR strategy [3], particularly when Crs is preserved and low Vt may be less beneficial. Recently, a nascent concept of "chemical power" has arisen illustrating the relevance of avoiding high intraoperative inspiratory oxygen (FiO_2) concentrations [22]. Although further validation in pre-clinical studies is required, avoiding very high FiO_2 (> 80 to 90%) still seems to be a reasonable approach.

In summary, intraoperative ventilation should be tailored to each patient rather than follow a "one-size-fits-all" approach (Fig. 1, panel B): anesthesiologists should aim to minimize DP and adjust PEEP to maintain alveolar recruitment while avoiding both collapse and overdistension. A Vt of 8 mL/kg PBW is often acceptable, and DP monitored via plateau pressure after a 1-s end-inspiratory pause. If DP exceeds a relatively safe range (often considered > 11–14 cmH_2O), Vt should be reduced while avoiding excessive RR. Future studies provide more insight into the impact of higher RR, as well as differential relevance of these strategies for specific patient populations, such as those undergoing one-lung ventilation.

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